REMARKS

Claims 1-18 are currently pending in the application. Claims 2, 3, 5, and 6 are amended, as set forth above. New claims 7-18 have been added.

In the recent office action, objections were made to misspellings in the specification and claims. Claim 5 was rejected under 35 U.S.C. §112, first and second paragraph, on grounds of lack of written description and indefiniteness. Claims 1-4 and 6 were rejected under 35 U.S.C. §103(a) on grounds of obviousness, in view of various prior art references. Each ground for objection and rejection is summarized below.

In view of the above claim amendments and the remarks below, Applicant respectfully requests reconsideration and withdrawal of the outstanding objections and rejections.

Brief Summary of the Claims

The claims in the present application are directed to methods for producing 2-chloro-2'-deoxyadenosine (CldAdo). In general, the methods include the following steps:

(a) converting a 6-oxo group of protected 2'-deoxyguanosine into a 6-leaving group;
(b) replacing the 2-amino group with a 2-chloro group;
(c) replacing the 6-leaving group with a 6-amino group; and
(d) removing the protecting groups, to produce 2-chloro-2'-deoxyadenosine.

New claims 7-18 include two new dependent claims which depend from each of the independent claims 1-6. The first of the two new dependent claims requires that the 2-amino group replaced with a 2-chloro group is performed using acetyl chloride and benzyltriethylammonium nitrite. The second dependent claim requires that the replacement of the 2-amino group with a 2-chloro group is performed at or less than f 0° C. Support for the dependent claims may be found at page 8 of the specification (submitted March 25, 2005), as well as Example 4 (pp. 13-14), and Figures 1 and 2.

While previous methods of synthesizing 2-chloro-2'-deoxyadenosine are known, the Applicant has discovered improved methods of efficiently synthesizing this medicinal compound.

Objections to the Specification

The examiner has identified spelling errors occurring in the specification. The misspellings are from two different documents: the specification upon entry of the application under 35 U.S.C. §371 and the substitute specification filed with a Preliminary Amendment on March 25, 2005. Applicant believes the substitute specification has been entered by the office; therefore, the present amendment to the specification corrects misspellings with reference to the substitute specification. If, however, the substitute specification has not been entered, Applicant respectfully requests entry of the substitute specification as filed on March 25, 2005. If there is any question regarding these issues, the examiner is invited to contact the Applicant's attorney to resolve these issues.

Applicant acknowledges the examiner's suggestion to modify the headings in the patent specification. Applicant's present amendment to the specification follows the guidelines as set forth in 37 C.F.R. §1.77(b). Section headings that have not, however been added are not relevant or applicable.

Objections to the Claims

The examiner has also objected to claims 3 and 5 which have minor spelling errors. The present claim amendments correct those spelling errors. A similar objection was made to claim 1 that "diazaotization/chloro-dedi[a]azoniation" was misspelled. Applicant amended claim 1 by preliminary amendment on March 25, 2005, and deleted the extraneous occurrence of "a" as indicated by brackets in the amendment. (*See* Preliminary Amendment, March 25, 2005 at p. 13). Applicant believes that claim 1, therefore, has no spelling error. In any event, the present listing of the claim reflects the correct spelling of "diazotization/chloro-dediazoniation."

Claim Rejections Under 35 U.S.C. § 112

A. Written Description

Claim 5 was rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The office action states that the Applicant-recited support for the preliminary amendment of claim 5 (page 5, lines 5-7) on March 25, 2005, does not support the amendment. The office action also indicates that the examiner could only identify page 9, lines 2-4 as support for the "reactivity at the C6 position of the purine."

Applicant believes its citation of support for the amendment was incomplete and regrets the error. Furthermore, Applicant has amended claim 5 to specify that the 6-leaving group has *lesser* reactivity than that of the 2-amino group in a diazotization/chloro-dediazoniation displacement reaction instead of *greater* reactivity.

Support for the present amendment may be found at page 4, line 17 through page 9, line 5. For example, the specification, beginning at page 4, describes steps for functionalizing the C-6 position of 2'-deoxyguanosine (dGuo), for replacing the 2-amino group with a 2-halo (for example chloro), and replacing the C-6 functional group with an amino group. In the paragraphs that follow, Applicant described various conditions and examples of suitable C-6 functional groups which are not altered during diazotization/halo-dediazoniation reaction conditions (directed at the C-2 position) and which can be subsequently replaced by or altered to become an amino group. The specification, therefore, supports the present amendment.

As amended, step (a) in claim 5 requires "converting the 6-oxo group . . . into a 6-leaving group having lesser reactivity than that of the 2-amino group in a diazotization/chloro-dediazoniation reaction." In other words, the 6-leaving group must not be displaced or changed under the diazotization/chloro-dediazoniation reaction conditions. This is consistent with step (b) in which a chloro group replaces the 2-amino group and with step (c) in which an amino group replaces the 6-leaving group by selective ammonolysis.

For at least these reasons, amended claim 5 satisfies the written description requirement of 35 U.S.C. §112, first paragraph.

B. Indefiniteness

Claim 5 was also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The office action states that the 6-leaving group is vague and indefinite if it has a greater reactivity than the 2-amino group but does not react during a diazotization/chloro-dediazoniation reaction.

Applicant has amended claim 5 which obviates the rejection. As amendedm claim 5 recites that the 6-leaving group has *lesser* reactivity than that of the 2-amino group in a diazotization/chloro-dediazoniation displacement reaction. Support for the present amendment may be found at page 4, line 17 through page 9, line 5.

Applicant believes the amendment and cited section of the specification overcome the rejection. For at least these reasons, amended claim 5 satisfies the definiteness requirement of 35 U.S.C. §112, first paragraph.

35 U.S.C. §103(a) Obviousness Rejections

Claims 1-4 and 6 were rejected under 35 U.S.C. § 103(a) as being unpatentable in view of various prior art. M.P.E.P. 706.02(j) sets forth the standard for a Section 103(a) rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicant respectfully traverses each rejection as set forth below.

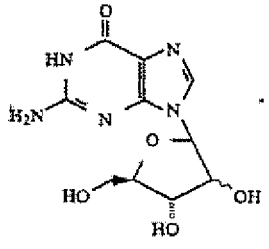
A. Claims 1, 2, and 4

Claims 1, 2 and 4 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,208,327 (hereafter "Chen"). The office action states that Chen discloses a process for converting guanosine to 2-chloroadenosine. The office action also states that Chen discloses the subsequent conversion of 2-chloroadenosine to 2-chloro-2'-deoxyadenosine. The office action correctly acknowledges, however, that Chen fails to disclose the conversion of 2'-deoxyguanosine to 2-chloro-2'deoxyadenosine. Nevertheless, the office has taken the position that the guanine moiety of guanosine may be substituted by 2'-deoxyguanosine. The office action concludes that it would have been obvious to change the sequence of steps disclosed by Chen.

Applicant respectfully traverses this rejection because Chen does not teach or suggest all of the claim limitations. It would not be obvious to substitute 2'-deoxyguanosine for guanosine as described by Chen, nor would it be obvious to change the sequence of steps disclosed by Chen.

1. Chen Fails To Teach or Suggest Starting With 2'-Deoxyguanosine

Chen does not disclose or suggest that guanosine may be substituted by 2'-deoxyguanosine in a process for synthesizing 2-chloro-2'-deoxyadenosine. Chen mentions "an analogue or derivative" of guanosine while describing the preparation of 2-chloroadenosine in scheme II. (*See* col. 6, l. 3). It is noteworthy that Chen's choice of words was "an analogue" (singular) not "analogs" (plural). Scheme II depicts compound F as guanosine and its arabino epimer analogue (reproduced below). This structure, thus, represents what Chen considered "an analogue" of guanosine.



F

As can be seen, compound F's stereochemistry at the 2' position is up or down (*R* or *S*). Guanosine, as mentioned by Chen at col. 6, ll. 43-44, is hydroxyl in the "down"

or 2'(*R*) orientation. Moreover, Chen identified the analogue of guanosine at col. 6, ll. 46-48: "the analogue of guanosine, i.e., compound F wherein the 2'-hydroxy is up." Two thing are noteworthy about this quotation. First, it refers to "the analogue" with a definite article "the" suggesting there was one and only one analogue. Second, Chen used the closed transitional expression "i.e." which means "that is" rather than the open transitional expression "e.g." which means "for example." Thus, one skilled in this art would consider the teaching of Chen to be limited to the compound 2-amino-9-((2*R*,3*S*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-1*H*-purin-6(9*H*)-one which is the arabino epimer of guanosine. (*Id.* citing *J. Med. Chem.*, 25(6), 1899 (1988)). One of ordinary skill in this art would not read Chen as suggesting any other analogue and would not, therefore, understand "an analogue" of guanosine to include 2'-deoxyguanosine.

Chen also identifies what constitutes a "derivative" of guanosine. Referring to scheme II, Chen calls compounds G and H "derivatives." (Col. 6, ll. 50-51). Compound G represents the C_1-C_5 alkyl or phenyl acyl derivatives of compound F. (Col. 6, ll. 53-56). Compound H represents the 2-amino-6-chloro derivative of peracylated guanosine. Consistent with the prior art teaching away from starting with 2'-deoxynucleosides, Chen never describes analogues or derivatives of guanosine as 2'-deoxy compounds.

In summary, Chen fails to describe or suggest using 2'-deoxyguanosine for the synthesis of 2-chloro-2'-deoxyadenosine. For at least these reasons, claims 1, 2, and 4 are not obvious in view of Chen.

2. Chen Fails To Suggest the Sequence of Claims 1, 2, and 4

The office action states that it would have been obvious to change the sequence of steps disclosed by Chen. This, however, is not suggested or taught by Chen. Furthermore, the claimed sequence achieves a synthetic yield markedly greater than the synthetic yield disclosed by Chen. This surprising and unexpected improvement demonstrates that the claimed sequence is nonobvious.

Chen discloses the synthesis of 2-chloroadenosine from guanosine over the course of 4 steps. (*See* col. 6, ll. 1-68). Chen also discloses the synthesis of 2-chloro-2'-deoxyadensoine from 2-chloroadenosine over the course of 4 additional steps. (*See* col. 3, l. 60 – col. 5, l. 68). The corresponding yield for this process as derived from the

examples is less than 3% (derived by multiplying the synthetic yield of each step reported in examples 1-8). In contrast, the Applicant's disclosure indicates that an overall yield of 64-75% was achieved in synthesizing 2-chloro-2'-deoxyadenosine from 2'-deoxyguanosine. (*See* page 11, lines 4-12, of the substitute specification). Applicant's processes involve fewer steps. Thus, using the claimed methods, the Applicant was able to achieve a markedly greater yield of 2-chloro-2'-deoxyadenosine compared to the method of Chen and with fewer steps. This improvement constitutes objective evidence that the claimed processes are nonobvious. For at least these reasons, claims 1, 2, and 4 are not obvious in view of Chen.

B. Claims 3 and 6

Claims 3 and 6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chen as applied to claims 1, 2 and 4 above and further in view of U.S. Patent No. 5,668,270 (hereafter "Bauman"). The office action states that Chen discloses a process for converting guanosine to 2-chloroadenosine where an intermediate step involves conversion of the 6-oxo group to a 6-chloro group. The office action correctly acknowledges, however, that Chen fails to disclose the conversion of a 6-oxo group to a 6-leaving group where the 6-leaving group is a 6-O-sulfonyl leaving group. The office action further states that Bauman teaches the conversion of the 6-oxo group of guanosine to a 6-O-sulfonyl leaving group. The office action concludes that it would have been obvious to substitute the halo leaving group of Chen with the 6-O-sulfonyl group disclosed by Bauman.

Notwithstanding the statements in Bauman, the obviousness rejection of claims 3 and 6 are improper because neither Chen nor Bauman teach or suggest all of the claim limitations. Both claims 3 and 6 include the limitation that the claimed processes start from protected 2'-deoxyguanosine. As stated above, Chen does not teach or suggest the synthesis of 2-chloro-2'-deoxyadenosine from 2'-deoxyguanosine. Furthermore, Bauman does not teach or suggest this limitation. Accordingly, the prior art cited in the office action fails to teach all of the limitations of claims 3 and 6. The claims, therefore, are not obvious.

SUMMARY

The pending claims and application, as amended, are patentable. Applicant respectfully requests the examiner grant early allowance of this application. The examiner is invited to contact the undersigned attorneys for the Applicant via telephone if such communication would expedite this issuance of this application.

Respectfully submitted,

/Ryan L. Marshall/
Ryan L. Marshall
Registration No. 47,770
Attorney for Applicant
BRINKS HOFER GILSON & LIONE
405 South Main Street, Suite 800
Salt Lake City, Utah 84111-3400
Telephone: (801) 355-7900
Facsimile: (801) 355-7901

April 4, 2008